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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,867	12/13/2001	Kevin P. Baker	P2830P1C60	6854

35489 7590 04/12/2005

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EXAMINER	
NICHOLS, CHRISTOPHER J	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,867	BAKER ET AL.	
	Examiner	Art Unit	
	Christopher J. Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,38-40 and 44-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33,38-40 and 44-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 April 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1.14.05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Amendment filed 14 January 2005 has been received and entered in full.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

3. The Objection to the Specification as set forth at pp. 2 ¶2 in the previous Office Action (14 July 2004) is hereby *withdrawn* in view of Applicant's amendments (14 January 2005).

4. The Rejection of claims **28-47** under 35 U.S.C. §112 ¶1 as set forth at pp. 18-27 ¶10-29 in the previous Office Action (14 July 2004) is *withdrawn* in view of Applicant's amendments (14 January 2005).

5. The Rejection of claims **28-33, 35-37,** and **41** under 35 U.S.C. §112 ¶2 as set forth at pp. 27-28 ¶30-32 in the previous Office Action (14 July 2004) is *withdrawn* in view of Applicant's amendments (14 January 2005).

6. The Rejection of claims **41-43** under 35 U.S.C. §112 ¶2 as set forth at pp. 28-30 ¶33-38 in the previous Office Action (14 July 2004) is *withdrawn* in view of Applicant's amendments (14 January 2005).

7. The Rejection of claims **28-39** and **41-47** under 35 U.S.C. §102(a) as set forth at pp. 30 ¶39-42 in the previous Office Action (14 July 2004) is *withdrawn* in view of Applicant's amendments (14 January 2005). The priority date for the instant application is 29 October 1999.

Maintained Objections And/Or Rejections

Oath/Declaration

8. The Objection to the Oath/Declaration as set forth at pp. 2 ¶3 in the previous Office Action (14 July 2004) is hereby *maintained.*

9. Applicant's arguments filed 14 January 2005 have been fully considered but they are not persuasive. 37 C.F.R. 1.52(c)(1) requires that:

Any interlineation, erasure, cancellation or other alteration of the application papers filed must be made before the signing of any accompanying oath or declaration pursuant to § 1.63 referring

to those application papers and should be dated and initialed or signed by the applicant on the same sheet of paper. Application papers containing alterations made after the signing of an oath or declaration referring to those application papers must be supported by a supplemental oath or declaration under § 1.67. In either situation, a substitute specification (§ 1.125) is required if the application papers do not comply with paragraphs (a) and (b) of this section. [emphasis added]

10. Applicant failed to note the conjunction of "dated" and "initialed" as one unit. The section conjunction of "or" separates the two units of "dated and initiated" and "signed". Furthermore, Applicant cannot argue defects in the Oath/Declaration. The alterations were not dated and initialed. The signature and date concerns the Oath/Declaration proper and not alterations which are covered by 37 C.F.R. 1.52(c).

Claim Objections

11. Claim **48** is objected to because of the following informalities: typos "of an at", "use". Appropriate correction is required.

12. Claim **48** is objected to because of the following informalities: the use of "a complement" makes it unclear which complement is claimed. Appropriate correction is required.

Maintained Rejections And as Necessitated by Amendment

Claim Rejections - 35 USC § 101

and

Claim Rejections - 35 USC § 112

13. Claims **33, 38-40,** and **44-53** are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a well-asserted utility or a well established utility for the reasons as set forth at pp. 2-17 ¶4-8 in the previous Office Action (14 July 2004).

14. Claims **33, 38-40,** and **44-53** are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a well-asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention for the reasons as set forth at pp. 18 ¶9 in the previous Office Action (14 July 2004).

15. Applicant traversed the rejection of the claims on the following grounds: **(a)** Example 143 (Table 8) explicitly discloses the biological activity of the nucleic acid of SEQ ID NO: 281 as being amplified in lung tumor tissue and therefore a diagnostic maker for lung cancer, **(b)** Declaration by Dr. Audrey Goddard, **(c)** Declaration by Dr. Avi Ashkenazi, and **(d)** the Specification provides a lengthy description on how to make and use the polynucleotide of SEQ ID NO: 281.

16. Applicant's arguments have been taken into consideration and are not found persuasive for the following reasons.

17. On "**(a)**", a deficiency under the "useful invention" requirement of 35 U.S.C. §101 arises where it is not apparent why the invention is "useful." This occurs when an Applicant fails to identify any specific and substantial utility for the invention or fails to disclose enough

information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention. *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966); In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993). This is the instant case. SEQ ID NO: 281 is elevated in a relative, non-quantitative assay of genes from a lung tumor sample. Overexpression of a single gene is not necessary or sufficient to indicate whether the tumor is malignant or benign, establish vascularization, or its potential for metastasis (all critical factors when evaluating a tumor). In addition, the commercially available tumor tissues used in the Specification lack any detailed information about the tumors used.

18. This instant assertion is firstly not specific because Applicant has not made a positive assertion of the polynucleotide of SEQ ID NO: 281's or the polypeptide of SEQ ID NO: 282's identity. The art teaches that two classes of genes and their proteins are involved in tumors (cancer): tumor suppressor genes and proto-oncogenes. Tumor suppressor genes are a class of genes (i.e. p53) that act in normal cells to inhibit unrestrained cell division and that when inactivated (as by mutation) place the cell at increased risk for malignant proliferation (also called *antioncogenes*) Proto-oncogenes are normal genes that have the potential to become an oncogene which in turn cause the transformation of normal cells into cancerous tumor cells. The polynucleotide of SEQ ID NO: 281 have not been positively identified as falling into either of these categories. Nor is the actual identity of the nucleic acid of SEQ ID NO: 281 or the polypeptide of SEQ ID NO: 282 been taught.

19. Secondly, the instant assertion is not substantial because the Specification is silent as to the identity of polynucleotide of SEQ ID NO: 281. Thus it would constitutes additional experimentation to first determine the identity of polynucleotide of SEQ ID NO: 281, then to

determine the use the nucleic acid of SEQ ID NO: 281. Therefore, the specification's assertion that the polynucleotide of SEQ ID NO: 281 is involved in lung tumors and/or cancer is not a substantial assertion of utility, since significant further research would be required of the skilled artisan to determine what its properties are. Nor is the assertion specific, as teaches the wide sequence variance and diverse tissue distribution of both classes of tumor related proteins and genes. Therefore this utility is neither specific nor substantial.

20. On "**(b)**", the Declaration under 37 CFR §1.132 by Dr. Goddard filed 14 January 2005 is insufficient to overcome the rejection of claims **33, 38-40,** and **44-53** based upon lack of utility and lack of enablement as set forth in the last Office action. At page 12 (14 January 2005), Applicants discuss the accuracy of the Taq DNA polymerase assay, stating that the Taqman PCR technique is sensitive enough to detect at least a 2-fold increase in gene copy number (paragraph 3) and that this increase is significant and useful. This argument has been fully considered but is not deemed persuasive because it evinces that the instant specification provides a mere invitation to experiment, and not a readily available utility.

21. The PRO1780 gene (nucleic acid of SEQ ID NO: 281 and amino acid of SEQ ID NO: 282) has *not* been associated with tumor formation or the development of cancer, nor has it been shown to be predictive of such. The specification merely demonstrates that the nucleic acid of SEQ ID NO: 281 was amplified in some lung tumor tissue, to a minor degree (about 2.5 fold). No mutation or translocation of PRO1780 has been associated with any type of cancer versus normal tissue. It is not known whether PRO1780 is expressed in corresponding normal tissues, and what the relative levels of expression are. In the absence of any of the above information, all that the specification does is present evidence that the DNA encoding PRO1780 is amplified in a

variety of samples, including some normal tissues, and invites the artisan to determine the significance of this increase. One cannot determine from the data in the specification whether the observed "amplification" of nucleic acid is due to increase in chromosomal copy number, or alternatively due to an increase in transcription rates. It remains that the issue is simply not predictable, and the specification presents a mere invitation to experiment.

22. Furthermore, the Declaration does not provide data such that the examiner can independently draw conclusions. Only Dr. Goddard's conclusions are provided in the declaration. It is noted that the literature cautions researchers from drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. For example, Hu *et al.* (July-August 2003) "Analysis of genomic and proteomic data using advanced literature mining." J Proteome Res. **2**(4): 405-12 analyzed 2286 genes that showed a greater than l-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column) and discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section).

23. In the instant case, the specification provides data showing a very small increase in DNA copy number-about 2.3 fold- in a two different types of tumor. However, there is no evidence regarding whether or not PRO1780 mRNA or polypeptide levels are also increased in this cancer. Furthermore, what is often seen is a *lack* of correlation between DNA amplification and increased peptide levels. This is discussed by Haynes *et al.* (August 1998) "Proteome analysis:

biological assay or data archive?" Electrophoresis. **19**(11): 1862-71 who teaches that polypeptide levels cannot be accurately predicted from mRNA levels, and that, according to their results, the ratio varies from zero to 50-fold (page 1863). The literature cautions researchers against drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue.

24. Given the small increase in DNA copy number of PRO1780, and the evidence provided by the current literature, it is clear that one skilled in the art would not assume that a small increase in gene copy number would correlate with significantly increased mRNA or polypeptide levels. Further research needs to be done to determine whether the small increase in PRO1780 DNA supports a role for the peptide in the cancerous tissue; such a role has not been suggested by the instant disclosure. Such further research requirements make it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. As discussed in *Brenner v. Manson*, (1966, 383 U.S. 519, 148 USPQ 689), the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and, "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

25. Accordingly, the Specification's assertions that the claimed antibodies which bind the polypeptide of SEQ ID NO: 282 (PRO1780) have utility in the fields of cancer diagnostics and cancer therapeutics are not substantial.

26. On "**(c)**", the Declaration under 37 CFR 1.132 by Dr. Ashkenazi filed 14 January 2005 is insufficient to overcome the rejection of claims **33, 38-40,** and **44-53** based upon lack of utility and lack of enablement as set forth in the last Office action. In the Declaration filed under 37 CFR 1.132, Dr. Ashkenazi claims that the purpose of the experiments that measured increases in gene copy number was to identify tumor cell markers useful for cancer treatment (pp. 1) and to identify cancers for which there was an absence of gene product over-expression (pp. 2).

27. The Ashkenazi declaration filed under 37 CFR § 1.132 argues that, even when amplification of a gene in a tumor does not correlate with an increase in polypeptide expression, the absence of the gene product over-expression still provides significant information for cancer diagnosis and treatment. This has been fully considered but is not found to be persuasive. No evidence is present as to whether the gene products (such as the polypeptide) are over-expressed or not. Further research is required to determine such. Thus, the asserted utility is not substantial.

28. Furthermore, Sen (January 2000) "Aneuploidy and cancer." Curr Opin Oncol. **12**(1): 82-88 teaches that chromosome aberrations known as aneuploidy are commonly observed in tumors. Whether aneuploidy is a cause or consequence of the tumor is unclear. While widespread in human tumors, the cancer cells show great phenotypic diversity in morphology, proliferation, antigen expression, drug sensitivity, and metastasis (pp. 82). Many tumor cells are aneuploid thus most have multiple chromosomes. Accordingly, gene copy number may be due to abnormal chromosome number, duplication, or fragmentation therefore not indicative of particular relevance to the genes encoded therein. Also, gene copy number does not predictably influence protein levels. In the instant application, the absence of follow-up experiments explaining the

expression of the instant polynucleotide of SEQ ID NO: 281 in the lung tumor tissue. Without a minimal knowledge as to what an appropriate level or activity of the polynucleotide of SEQ ID NO: 281 is in healthy normal appropriate control tissue and how they would differ in pathological tissue afflicted with specific diseases, the finding of the absence or presence of the polynucleotide of SEQ ID NO: 281 in tissue does not provide artisans with any workable information they could act on in a diagnostic fashion because the instant disclosure does not present a persuasive case that the polynucleotide of SEQ ID NO: 281 is significantly altered in any way in any pathology. The only working example in this regard offered by the specification indicates that the polynucleotide of SEQ ID NO: 281 is overexpressed in an unidentified lung tumor sample. The results provided by the disclosure of overexpression of the polynucleotide of SEQ ID NO: 281 in lung tumors may be the result that either is normally expressed in these tissues, but not expressed or expressed at a lower level in other tissues. Therefore substantial further research by the skilled artisan is required to determine how to use the antibody in the asserted utility to detect tumors. The asserted utility is also not specific, since the entire class of antibodies can be asserted to be used in this way.

29. On "**(d)**", the instantly claimed invention fails to satisfy the requirements of 35 U.S.C. §101 and §112 ¶1 because it does not have a credible, specific, and substantial utility. While the instant Specification teaches how to make the instantly claimed nucleic acids, it does not satisfy the second requirement of 35 U.S.C. §112 ¶1 which is "how to use" the invention.

30. The instant disclosure is silent as to the actual biological activity or function of the polynucleotide of SEQ ID NO: 281. Without some minimal teaching as to the amount or level of activity of the polynucleotide of SEQ ID NO: 281 in either a normal or disease state, the artisan

is without guidance or direction as to what any change in amount or level of activity of the polynucleotide of SEQ ID NO: 281 would indicate and what therapeutic course of action should follow. For example, it is completely unknown if a rise in the level or activity of the polynucleotide of SEQ ID NO: 281would indicate in a cancerous tissue. And if so, it is not taught whether this rise in the polynucleotide of SEQ ID NO: 281 needed to be suppressed, under the assumption that the polynucleotide of SEQ ID NO: 281 was somehow causative or contributory to the pathology of cancer. In the alternative, a rise in the polynucleotide of SEQ ID NO: 281 could indicate that the tissue was attempting to combat the cancer by activating tumor suppressing genes (an example known in the art of a tumor suppressing gene is p53). In which case, the artisan would desire to further increase the activity or level of the polynucleotide of SEQ ID NO: 281 and not suppress or inhibit it. Because the instant application does not provide some minimal context as to what altered levels of the polynucleotide of SEQ ID NO: 281 mean the artisan can find no therapeutic utility for the claimed nucleic acid because significant and substantial further research would need to be performed in order to answer these simple but vital questions. Without an answer to these vital questions, no meaningful therapeutic administration of the claimed nucleic acid can be accomplished without the minimal knowledge of whether increased or decreased levels or activities of the polynucleotide of SEQ ID NO: 281 was a deleterious or beneficial biological event.

31. Therefore, it is not clear how the skilled artisan would use the claimed nucleic acids for therapeutic uses. Since there is no substantial utility for the encoded polypeptide, there is also no substantial utility for the nucleic acid to identify such in any given purification methodologies. It would take significant further research to determine if the instantly claimed nucleic acid could be

used as for particular purpose, since no nexus between a disease state, condition, expression pattern, function, mutation, or activity has been disclosed in the specification. As significant further research would be required to determine how to use the claimed nucleic acid, the asserted utility is not substantial. In addition, this utility may be asserted for any given nucleic acid and thus it is not specific.

32. Claims **48-53** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

33. The claims are drawn very broadly to an isolated nucleic acid comprising the SEQ ID NO: 281 polynucleotide and fragments thereof. The language of said claims encompasses sequence variants, fragments, chemical derivatives, fusion proteins, tagged proteins, and chimeric proteins encoded by the isolated nucleic acid and its fragments.

34. The specification teaches that the nucleic acid of the SEQ ID NO: 281 polynucleotide sequence encodes the protein of the SEQ ID NO: 282 amino acid sequence (therein notated as "PRO1780" and "DNA71169-1709").

35. However, the specification fails to provide any guidance for the successful production, isolation, and characterization of isolated nucleic acid comprising the SEQ ID NO: 281 polynucleotide sequence or any variants, derivatives, and fragments thereof. The claims also encompass fragments and complements that hybridize to the nucleic acid of SEQ ID NO: 281. The resolution of the various complications in regards to predicting protein structure, function,

and nature purely based on sequence prediction is highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed would require the *de novo* production, isolation, and characterization the nucleic acid comprising the SEQ ID NO: 281 polynucleotide sequence, variants, derivatives, and fragments thereof to an established identity and function. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

36. Additionally, a person skilled in the art would recognize that predicting the efficacy of using sequence homology alone to predict the structure, nature, and function of the nucleic acid comprising the SEQ ID NO: 281 polynucleotide sequence, variants, derivatives, and fragments thereof as highly problematic (see MPEP §2164.02). Thus, although the specification prophetically considers and discloses general methodologies of producing, isolating, and characterizing the nucleic acid comprising the SEQ ID NO: 281 polynucleotide sequence, variants, derivatives, and fragments thereof, such a disclosure would not be considered enabling since the state of protein biochemistry is highly unpredictable and complex. The factors listed below have been considered in the analysis of enablement [see MPEP §2164.01(a) and *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)]:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

37. The following references are cited herein to illustrate the state of the art of protein biochemistry.

38. Regarding derivatives and fragments of isolated nucleic acid comprising the SEQ ID NO: 281 polynucleotide sequence, variants, derivatives, and fragments thereof and the polypeptides encoded therein, the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry **29**(37): 8509-8517; Ngo *et al.* (2 March 1995) "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 433-506]. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the

nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research **10**:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. **18**(1): 34-39, especially p. 36 at Box 2; Doerks *et al.* (June 1998) "Protein annotation: detective work for function prediction." Trends in Genetics **14**(6): 248-250; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature Biotechnology **15**:1222-1223; Brenner (April 1999) "Errors in genome annotation." Trends in Genetics **15**(4): 132-133; Bork and Bairoch (October 1996) "Go hunting in sequence databases but watch out for the traps." Trends in Genetics **12**(10): 425-427]. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art

which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

39. Thus the specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of applying results from *sequence homology predictions* and *hybridization conditions* to the actual structure, function, and nature of the nucleic acid comprising the SEQ ID NO: 281 polynucleotide sequence, variants, derivatives, and fragments thereof as exemplified in the references herein.

40. Claims **48-53** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not contain a written description of variants, derivatives, fragments, complements, or hybrizidable fragments of the claimed polynucleotide.

41. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

42. With the exception of the nucleic acid of the SEQ ID NO: 281 polynucleotide sequence, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

43. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

44. Therefore, only isolated polypeptides comprising the *nucleic acid* sequence set forth in SEQ ID NO: 281, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

45. Claims **48-53** are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier *et al.* (EST 09-March-1998) "WashU-NCI human EST Project".

46. Hillier *et al.* discloses a nucleic acid which shares 100% homology with SEQ ID NO: 282 for 373 bp and therefore is "a complement of" SEQ ID NO: 281 thus meeting the limitations of claims 48-53 (see Sequence Listing).

Summary

47. No claims are allowed.

SHARON TURNER, PH.D.
PRIMARY EXAMINER
3-29-05

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is **(571) 272-0889**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback** can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

CJN
March 28, 2005